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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,390	02/12/2001	Samuel T. Labrie	PF-0232-1 DIV	8952

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INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 04/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 12/17/02

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-21 is/are pending in the application.
Of the above, claim(s) 3-15, 18-21 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1, 2, 16, 17 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) 1-21 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-404-496/40517

Part III: Detailed Office Action

Claims 1, 2, 16 and 17 are under consideration. Applicant's request for rejoinder is noted but is held in abeyance, there being no allowable claims.

Objections and Rejections under 35 U.S.C. §§101 and 112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 16 and 17 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for reasons cited in the previous Office Action, paper number 7 mailed 9/24/02, at page(s) 3-4.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 16 and 17 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants traversal in paper number 8 filed 12/17/02 has been fully considered but is not deemed persuasive.

Beginning at page 8 of the response, applicants argue that there is a "well-established" utility for the claimed invention in toxicology testing, drug development and disease diagnosis through gene expression profiling. This same line of argument is continued beginning at page 10, with reference to papers by Rockett et al., Nuyasir et al., and Steiner et al. Beginning at page 15, applicants argue that the uses of NHG in toxicology testing, drug discovery and disease diagnosis are practical uses beyond mere study of the invention itself. This argument has been fully considered

but is not deemed persuasive.

Beginning at page 9 of the response, applicants argue that the precise biological role or function of an expressed polypeptide is not required to demonstrate utility.

Note that, contrary to appellants assertion, there is no requirement being made by the Examiner that the "biological function" of the claimed polynucleotides be known to establish utility. It is noted that "biological function" may mean many things, including the ability to encode protein. The Examiner interprets "biological function" in this context to mean the actual activity of the protein encoded by the claimed nucleic acid, or the actual activity of the nucleic acid itself, if it does not encode protein. Biological function is one of the factors that might be disclosed in establishing utility, but it is not required. Note that determination of the significance of the presence of the claimed nucleic acid in relationship to diagnosis, treatment or prevention of a developmental, cell proliferative or immunological disorder would not require any knowledge of biological function; the mere correlation of the presence of the nucleic acid, in a manner that would be found to be credible by a person of ordinary skill in the art, with the presence of a disease or condition would clearly meet the requirements of 35 U.S.C. § 101. Thus, appellants statement that there has been a requirement made that appellants disclose the biological function of the claimed nucleic acid is incorrect.

Arguments at pages 11-12 relate to the use of a database comprising sequences of expressed genes (it is not clear whether SEQ ID NO: 1 was in that database). This line of argument is again picked up at page 14, where applicants stress that a "vibrant market has developed for databases containing all expressed genes, in particular genes having medical and pharmaceutical significance such as the instant sequence." This argument has been fully considered but is not deemed persuasive because what is being claimed here is a protein, whereas the databases in question contain nucleic acid sequence information, which is an informational representation of nucleic acids. Neither the protein sequences nor the proteins themselves form the 'database'.

Beginning at page 12, applicants discuss a declaration by Dr. Furness. The declaration under 37 CFR 1.132 filed 12/17/02 (the Furness declaration) is insufficient to overcome the rejection of claims under 35 U.S.C. § 101 and 112, first paragraph as set forth in the last Office action because:

At paragraph 6, Dr. Furness asserts that the person of ordinary skill in the art would have considered the priority application to have disclosed the use of SEQ ID NO: 1 "as a research tool in a number of gene and protein expression monitoring applications that were well-known at that time to be useful in connection with the development of drugs and the monitoring of the activity of such drugs." At paragraph 9, Dr. Furness states that his consideration of utility focuses on the use of the protein of SEQ ID NO: 1 in gene and protein expression monitoring applications. At paragraph 10, Declarant discusses the prior art with respect to using 2-D PAGE mapping to study regulation of protein expression by drugs and toxic agents.

At page 21, the specification teaches that "A variety of protocols for detecting and measuring the expression of NHT, using either polyclonal or monoclonal antibodies specific for the protein are known in the art." At page 45, the use of the protein (or antibodies thereto) for diagnostic or drug screening techniques is discussed. There is no disclosure of the use of the protein in the type of drug development and toxicology testing urged by Dr. Furness. Utility must be in the form of a specific and substantial *disclosed* utility, or a well-known utility. Further, well-known utility must be specific and substantial. Examples of well-known utilities of protein include, for example the use of insulin in treatment of diabetes. The use of the claimed protein for 2-D PAGE in toxicology testing or drug development does not meet the requirements of 35 U.S.C. § 101 because (a) the use is not well-known, that is, is not of the level of well-known use such as the use of insulin (b) cannot be asserted for *any* protein, and was not asserted for the protein of SEQ ID NO: 1, and (c) does not require the isolation of the protein of SEQ ID NO: 1. Assuming, *in arguendo*, that the drug discovery and toxicology testing discussed in the declaration are "well-known utilities", they would still not satisfy the requirements of 35 U.S.C. 101 and 112, first paragraph, since well-known utilities must also be specific and substantial. Since the type of testing discussed by Dr. Furness can be done

with any new, uncharacterized protein, the asserted utility is not specific. Also, since the specification does not disclose a correlation between any disease state and an alteration in level or form of protein of SEQ ID NO: 1, significant further experimentation would be required of the skilled artisan to establish such a correlation. Thus, these utilities are also not substantial." Further, the uses urged by declarant do not require isolated protein of SEQ ID NO: 1: In the type of analyses urged by Declarant, the proteins themselves are not isolated, nor are antibodies to specific proteins made. Rather, cells are exposed to agents, then cell extracts made, and analyzed to see which "spots" are found on the gel. The methods do not use isolated proteins. Thus, unlike nucleic acid microchips, wherein specific nucleic acid probes must be isolated and affixed to the microchip used in the analysis, the type of analysis argued by Declarant does not require isolated proteins such as that claimed.

At paragraph 12, Declarant argues that given the disclosure that expression of the protein of SEQ ID NO: 1 is associated with brain, neuronal and lymph node tissues, that it would have led the person of ordinary skill in the art working on developing new drugs for the treatment of appetite and eating disorders, especially anorexia, cachexia and obesity to conclude that a 2-D PAGE map containing the protein of SEQ ID NO: 1 would be more useful than one without. This argument has been fully considered but is not deemed persuasive because as stated above, the PAGE maps are not made using purified samples of individual proteins, but rather are a representation of the total protein content of the cell. Further, since the specification does not establish that the protein of SEQ ID NO: 1 is expressed in any eating disorder in any way that is different from the way it is expressed in normal individuals. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify diseases states which correlate with altered levels or forms of the claimed protein. Therefore, this asserted utility is also not substantial.

It is noted that applicants and Declarant refer to NHT as a "novel tubby homologue. The art-accepted meaning of "homologues" as applied to proteins, is that when two proteins are "homologues" of each-other, they represent the same protein as it is found in two different

organisms, or alternatively two proteins from the same organism, that are evolutionarily derived from a common ancestral protein. See for example the definition of the term "homologous" in Modern Genetics (*F. Ayala et al.*, Benjamin Cummings, Menlo Park, 1980), which defines the term as meaning "of genes and structures that are similar in different organisms owing to their having inherited them from a common ancestor." As an example of the former, human insulin and bovine insulin do not have the exact same amino acid sequence, but serve the same biological function in their respective hosts, and are considered to be "homologues". An example of the latter is found in lens crystallin proteins. As stated by Wistow et al. (Nature 326:622-625, 1987) "Because of the relatively recent evolutionary origin of the lens, it has been recognized that is protein components are probably derived from non-lens ancestors. This has been verified for the α-crystallins which belong to the same protein superfamily as the small heat shock proteins, whereas the β and γ-crystallins are related to each other, and also to protein S, a calcium-binding protein of the bacterium *Myxococcus xanthus*." Thus, within organisms, proteins diverge evolutionarily to take on different functions, such as heat shock proteins evolving into lens crystallins. While TUBBY and SEQ ID NO: 1 certainly share homology, i.e. they are have some level of sequence identity and structural similarity to each other, it is exceedingly unlikely that an organism (human) would evolve two different proteins (TUBBY and SEQ ID NO: 1) with significantly different amino acid sequences to serve the same biological function. What is much more likely is that the two proteins are evolved from a common ancestor, i.e. are evolutionarily related, and have diverged to serve substantively *different* functions, as with the heat shock proteins and lens crystallins. Accordingly, the person of ordinary skill in the art would not consider credible the assertion that SEQ ID NO: 1 would be expected to play the same role *in vivo* as TUBBY. Similarly, the assertions at page 2 of the specification are mere conjecture based upon expression patterns, and would also not be considered, in the absence of any confirmatory evidence, to be credible by a person of ordinary skill in the art.

Finally, Declarant asserts that one would use ELISA, RIA or FACS for measuring NHT, and thus that the protein has utility. This argument has been fully considered but is not deemed persuasive because such analysis, in the absence of any known role of NHT, is considered to be

further research on NHT itself, to determine the role, function and properties of the protein. Such use for further research does not meet the requirement of 35 U.S.C. § 101.

As an aside, it is noted that Dr. Furness is a consultant for Incyte Pharmaceuticals, Inc., the assignee in this application, and thus is a concerned party. Further, it is noted that no new facts or evidence on the role, function or properties of the claimed protein have been presented, thus the declaration appears to be largely one of opinion. The declaration has been considered with regard to the discussion of the state of the art, and what is actually disclosed. However, any legal conclusions therein are not entitled to any weight. See *In re Chilowsky*, 306 F.2d 908, 134 USPQ 515 (CCPA 1962) (expert opinion that an application meets the requirements of 35 U.S.C. 112 is not entitled to any weight; however, facts supporting a basis for deciding that the specification complies with 35 U.S.C. 112 are entitled to some weight); and *In re Lindell*, 385 F.2d 453, 155 USPQ 521 (CCPA 1967), and MPEP 716.01(c).

Beginning at page 16, applicants argue that "evidence that the claimed invention is a member of the TUBBY protein family would be found by one skilled in the art to be more likely than not true. This argument has been fully considered but is not deemed persuasive because, as explained above, mere structural relatedness is not predictive of function. As for lens crystallins, the mere assignment as being part of the "TUBBY protein family" on the basis of some level of structural similarity does not inform the person of ordinary skill in the art as to the function or significance of the protein.

Beginning at page 20, applicants assert that membership in a class of useful products can be evidence of utility. It is true that practical utility can be derived IF each and every member of the broad class possess (or would more likely than not) possess a common utility. Applicants argue that the Examiner has not provided evidence that any member of the TUBBY polypeptide family lacks utility. This is not the issue here. Merely identifying SEQ ID NO: 1 as belonging to the TUBBY family does not denote any specific, substantial and credible utility for the particularly claimed protein of SEQ ID NO: 1, because membership in the TUBBY family does not imply any disclosed common utility. Since there is no single utility common to members of the family, merely

identifying SEQ ID NO: 1 as a member of the family is insufficient to confer utility. The members of the family share some amino acid sequence similarity, however, they have very distinct three dimensional structures which accounts for them binding distinct receptors. Appellants have offered no evidence to support the assertion that all TUBBY proteins "convey practical benefit", and one of ordinary skill in the art would not agree that a common specific, substantial and credible utility is possessed by the family of TUBBY proteins, absent evidence to the contrary.

Beginning at page 21, applicants argue that NHT shares 99% sequence identity with TULP3, which has been demonstrated to function in signal transduction from heterotrimeric G protein-coupled receptors, and that this identity therefore confers utility to NHT. This argument has been fully considered but is not deemed persuasive because there is no evidence of record that the ability to "function in signal transduction from heterotrimeric G protein coupled receptors" constitutes a utility, nor that that utility was disclosed in the specification as originally filed. Further, the demonstration of TULP3 function occurred after the filing date of the instant invention; there is no evidence of record that applicants had conception of such activity at the time the instant invention was made.

At the paragraph bridging pages 23-24, applicants argue that the citations made by the Examiner to North et al., PNAS 94:3128 , who report that TULP1 and TULP2, which are 'tubby-like proteins' with 60-90% identity to TUBBY in their N-terminal portions, are likely to be associated not with appetite, but with ocular diseases, and Gu et al., Lancet 351:1103 who confirm that TULP1 mutations were found in 171 patients with retinitis pigmentosa, is not pertinent to NHT, as the expression patterns are different. This argument has been fully considered but is not deemed persuasive because the point of the citations by the Examiner was that there is no single recognized function for TULP proteins known at the time the invention was made, nor any commonality of expression patterns that would lead to expectation of common function in disease states.

Applicants repeated citation of a paper by *Santagata* et al. is noted. Santagata discloses that TUBBY proteins function as membrane-bound transcription regulators that translocate to the nucleus in response to phosphoinositide hydrolysis, providing a direct link between G-protein signaling and

the regulation of gene expression (abstract). However, it is noted that the publication date of Santagata et al., 2001 if post-filing date, and cannot be relied upon to establish what was known about TULP proteins at the time the invention was made. Further, as stated above, there is no evidence of record that the ability to "function in signal transduction from heterotrimeric G protein coupled receptors" constitutes a utility, nor that that utility was disclosed in the specification as originally filed.

Beginning at page 25, applicants argue that diagnosis and treatment of appetite and eating disorders are sufficient utilities under 35 U.S.C. § 101 and 112, first paragraph. This would be true if said treatments were considered to be a credible assertion. However, this argument has been fully considered but is not deemed persuasive because as stated in the original rejection, there is no credible link between the disclosed NHT and any known appetite or eating disorder. At the sentence bridging pages 25-26, applicants argue that they "have presented evidence that the claimed invention would have the utilities of TUBBY proteins, proteins which are known to be involved in appetite and eating disorders." This argument has been fully considered but is not deemed persuasive because as stated above, there is no common utility known for TUBBY proteins, nor is there any evidence of record that TUBBY proteins are " known to be involved in appetite and eating disorders."

Beginning at page 26, applicants argue that the Examiner, in implementing the PTO Utility Examination Guidelines, is requiring a "particular or unique utility", and that such is not consistent with the law. The Examiner has no authority to comment regarding applicant's citation of the Written Description and Utility Guidelines, nor the statements by Mr. Doll. However, it remains that applicants have presented no specific and substantial utility for the claimed invention. The Examiner is not requiring a "unique" utility; if, for example, SEQ ID NO: 1 were shown to have identical expression patterns to a known cancer marker, or to be a surrogate for a cell protein of interest in toxicology, that would, indeed constitute utility. However, such is not the case here. Here, appellants are urging that the use of the claimed protein in general methods which do not require any knowledge of the specific properties of the claimed protein is sufficient, although the

results of those uses would merely be useful for further research, or alternatively that the protein may be used to treat disorders for which there is no association to the claimed protein established. Cells express thousands of proteins. A mere identification that cells in a particular portion of the anatomy express a protein is not a causal link to any particular disorder that might involve that portion of the anatomy. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant invention has no utility and is not enabling because one cannot, following the guidance presented therein, use the claimed protein without first making a substantial inventive contribution, that is, without determining a property of the protein that would lend itself to a specific, substantial and credible use.

The Examiner reiterates that even if a credible link were established for the disclosed nucleic acids, such would not be sufficient to confer utility to the protein, as it is not recognized in the art that nucleic acid levels are predictive of protein levels. For example, see Haynes et al. (Electrophoresis 19:1862-1871, 1998), studied 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript levels; for some genes, equivalent mRNA levels translated into protein abundances which varied by more than 50-fold. Haynes concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (page 1863, 2nd paragraph, and Figure 1). Therefore, there is no specific, substantial and credible utility disclosed for the claimed protein and compositions, nor for antibodies that might be made using the claimed protein.

Beginning at page 29 of the response, applicants argue the issue of scope of enablement. Applicants argue that because the claims are limited to naturally occurring variants, that they must be functional (paragraph bridging pages 30-31). This argument has been fully considered but is not deemed persuasive because it is not clear what variants are intended; it is not true that naturally occurring variants must be functional, as it is just the lack of such function or alteration of such function that causes genetic disease. Applicants further argument that an assay for determining functionality has been disclosed at pages 43-44 of the specification is also not persuasive, as said assay is merely prophetic, and it is not predictable that the protein of SEQ ID NO: 1, much less variants thereof, would have activity in said assay.

Claims 1 and 16 also remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons cited in the previous Office Action paper number 7, at page(s) 6-7. Applicants arguments of this rejection, beginning at page 33 of the response, have been fully considered but are not deemed persuasive. Applicants have described only a single naturally occurring sequence, that of SEQ ID NO: 1. No other naturally occurring sequences have been described as obtainable from human, nor any other animal. A breadth of 90% would reasonably be expected to encompass homologues obtained from other primate species such as macaque, rhesus, gibbon, as well as from non-primate species, such as rat or mouse, giraffe, hippo, or even frog or yeast, depending upon the evolutionary conservation of the protein in question. Applicants have provided no information or description about how conserved the protein in question is, that is, how similar the homologues from other species would be expected to be, nor have they described a single species other than the single predicted protein based upon a nucleic acid obtained from a single human. There is no description of the function of the protein, such as would allow one of skill in the art to predict what portions of the disclosed sequence would be expected to be conserved. With

further respect to this issue, it is a protein that is being claimed; without having a written description of all naturally occurring sequences within the metes and bounds of the claims, one would not be capable of determining whether or not a given species was claimed.

At page 34, applicants argue that variants are described, for example, at pages 5 and 11 of the specification. This argument has been fully considered but is not deemed persuasive. Page 5 of the specification merely defines what a variant *is*. It does not describe even a single naturally occurring variant. Similarly, at page 11, the specification merely describes prophetically the percent identity that such variants might have to SEQ ID NO: 1, i.e. to give rise to 'naturally occurring' species within the scope of the claims. However, it is not true that one could find in nature any and all possible changes within a given protein, and the specification has described not a single naturally occurring variant of SEQ ID NO:1. Further, even *if* the specification had described some naturally occurring variants within the scope of the claims, such would not be commensurate in scope with the claims. This is because one of ordinary skill in the art would expect 10% variation to read on species homologues, that is, similar sequences as isolated from different biological species. There is not a single sequence disclosed that is obtained from another biological species.

At page 34, appellants argue that one of ordinary skill in the art would recognize naturally occurring variants of SEQ ID NO: 1 having 90% identity to SEQ ID NO: 1; this is not true. One could certainly determine whether a protein that one had obtained from nature were 90% identical to SEQ ID NO: 1, but that same person, handed a protein in a test tube, would have no way of determining whether that protein were 'naturally occurring'.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 16 and 17 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As no naturally occurring sequences having 90% identity to SEQ ID NO: 1 are described, the

metes and bounds of claim 1 cannot be determined. It cannot be determined which 90% identical sequences are or are not naturally occurring. Applicants argue that "
naturally occurring" would be understood by one of skill in the art to be that which occurs in nature. This argument has been fully considered but is not deemed persuasive because applicants are missing the point. The point of the rejection is that, were one handed a protein in a test tube, one could not determine whether or not that protein was within the metes and bounds of claim 1. Without a description of all naturally occurring proteins within the metes and bounds of the claim, a given isolated protein cannot be ascribed as being either naturally occurring or not naturally occurring. Accordingly, the claim is indefinite. Once a protein is made, it is not possible to determine how it was made, nor its original source (it is noted that the claim encompasses naturally occurring proteins that have been synthesized recombinantly or chemically, as well as those isolated from nature). The sequence and structural properties in no way reveal the origin of the molecule or its forebears.

Claims 2, 16 and 17 are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1 and 16 remain rejected under 35 U.S.C. 102(e) as being anticipated by Kleyn et al., U.S. Patent Number 5,646,040 for reasons cited in the previous Office Action.

Applicants argue that removal of "immunogenic fragments" and insertion of "said polypeptide retaining at least one function of a polypeptide comprising an amino acid sequence of

SEQ ID NO: 1" obviates this rejection. This argument has been fully considered but is not deemed persuasive because immunogenicity is a "function" of the protein of SEQ ID NO: 1, thus the amendment does not significantly change the scope of the claims, and the art continues to apply.

Advisory Information:

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector

Lorraine Spector, Ph.D.
Primary Examiner

09/782390.2
4/3/03